

Wilkie had said, they should get more power into their own lives as venereologists. They had tried their hardest during the war and were beaten down ; what they had achieved was remarkable in view of the opposition they were up against. As Dr. Flynn had said, in some general hospitals the matrons were often as difficult as the Commanding Officers were in others ; they seemed to have absolutely no appreciation of life, and certainly no desire to help in the cure.

Dr. Frankenberg had mentioned the squads which had been started first in Naples and continued in the British Liberation Army ; they had certainly done a lot of good, as long as they had kept up pressure on the civil authorities. Had the venereologists been able to undertake the treatment of contacts themselves, he felt sure that they could have done a lot more good than by leaving it to the civil authorities.

SIGNIFICANCE OF THE BLOOD WASSERMANN REACTION AFTER MALARIA THERAPY IN GENERAL PARALYSIS

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It has been found that in patients with general paralysis of the insane, treated with malaria alone or with malaria and chemotherapy combined, a large number of the blood Wassermann reactions remain positive. This fact may be a cause of considerable anxiety to the patient (if he be aware of it), to the relatives and to the physician. Furthermore, a great deal of time and money may be expended on an effort to render the Wassermann reaction negative. This article contains a report of two investigations bearing on the subject and an attempt to correlate these findings with other information available.

Somatic syphilis and general paralysis

In the first investigation the clinical records of 312 general paretics at Horton Hospital were examined for evidence of somatic syphilis. The patients had been under observation for periods varying from a few months to 15 years. Of the total number, 144 patients had died in the hospital and the remainder had been discharged. Thus clinical material representative of all stages of the disease was available. Of the group with a fatal outcome, 18 patients had not been treated with malaria ; all the others had been treated with malaria alone.

Clinical findings

Of the 312 cases, in 3 there were lesions suggestive of meningo-vascular syphilis or cerebral gumma. In these cases the diagnosis of general paralysis was doubtful. Of 6 congenital cases, in one there was syphilitic otitis and interstitial keratitis, in another choroiditis. In one there was a history of syphilitic rash, in another of jaundice. There were 2 clinical cases of aortic stenosis and 2 of aortic regurgitation. Another patient was discovered clinically and radiologically to have an early aneurysm of the aorta. In 3 cases ulcerated legs had been diagnosed as syphilitic, but there is a strong probability that the lesions were varicose. Two patients had ulceration of the soft palate ; in one the process involved the larynx and nasal septum.

Post-mortem findings (144 necropsies)

Out of a total of 144 post-mortem examinations, 23 cases of syphilitic aortitis were recorded. None of the patients concerned had complained during life of any symptoms referable to the aorta. One patient had an early aneurysm of the aorta. In one case a diagnosis of aortic regurgitation was made during life and confirmed *post mortem*. In this instance death appears to have been due to

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heart failure. All the other members of this group appear to have died primarily of generally paralysis of the insane.

Discussion

There were thus only 9 cases with evidently syphilitic lesions apart from neurological syndromes, namely, 7 cardiovascular lesions and 2 of the soft palate; the congenital cases and those of asymptomatic aortic disease are excluded. This is a proportion of somewhat less than 3 per cent.

The above figures probably do not give a correct indication of the number of cases of asymptomatic syphilitic aortitis first discovered at necropsy. Only the grosser degrees were recorded. This condition is very common indeed in paretics if all stages are taken into account. A number of patients in whom this lesion developed had received adequate chemotherapy—even when judged by the most rigorous standards—from the time of their primary lesion. It is worthy of note in this connexion that one explanation of Wassermann-fastness in latent syphilis which is frequently advanced is that of an undiscovered active lesion (Lord). It is thus possible that these aortic lesions, although of no great immediate importance, may be responsible for the persistently positive blood Wasserman reaction in paretics whose cerebrospinal fluid reactions have returned to normal, and in regard to whom it may be assumed that the brain lesion is no longer active.

The above findings, then, tend to confirm the view that gross tertiary lesions are rarely found in association with general paresis. The theory of the "neurotropic spirochaete" was based on this observation (Harrison). It should be observed, however, that tertiary lesions are increasingly rare in syphilis in general.

Thus the large proportion of Wassermann reactions remaining positive in paretics after malaria therapy bears no relation to the incidence of clinical tertiary lesions in these patients, nor is a case yet made out for regarding the possibility of such lesions as a major factor in determining our attitude to the persistently positive Wassermann reaction in these cases.

Moore has suggested that after malaria therapy without chemotherapy there may be an allergic change leading to a return to tertiary syphilis. This view is not borne out by the above findings nor by White's experience. Another observation made during the course of the present investigation strengthens the view that this is not a real danger. In cases of general paresis treated with malaria which show clinical improvement or arrest of the disease, the cerebrospinal fluid gradually returns to normal, whereas the blood Wassermann reaction does not do so at first. During the selection of cases for this investigation, however, it was noted that a number had become Wassermann-negative without further treatment several years after receiving malaria therapy.

Undoubtedly, further observation of cases treated with malaria alone, with particular reference to signs of tertiary syphilis, is desirable before any dogmatic statement is made. The above findings do demonstrate, however, that no case is made out for routine chemotherapy to prevent the development of tertiary lesions in general paretics after malaria. The other main reason advanced for the use of chemotherapy is, however, its necessity or desirability as an adjunct to malaria in the treatment of the paresis. This aspect of the problem was not covered in the present investigation, but the findings of Nicol and Hutton show that results obtained with malaria alone compare favourably with those in series in which chemotherapy was also used. Moore has suggested that arsenicals are desirable to complete the effect of quinine and prevent malaria relapse, but our experience at Horton Hospital has shown this to be necessary.

One final question which may be raised is that of infectivity. Does or does not the persistence of a positive blood Wassermann imply danger of transmission of the infection to the partner or offspring? In the group of 312 cases mentioned above, there was a history of miscarriages in 22 per cent of the women, that is to say, 1 miscarriage in 40 cases, 2 in 16, 3 in 7, and more than 3 in 7 cases. However, the extensive records accumulated at Horton show that most of these miscarriages occur during the early stages of the disease, and that children born

when the condition has already reached the neurological stage are free from infection. It was also the usual finding that when marriage occurs at a late stage in the disease the marital partner remains uninfected.

It may be concluded, then, at the present stage of our knowledge that chemotherapy during or after malaria therapy is not essential as a routine in general paralysis, although the persistence of a tertiary lesion may call occasionally for special measures.

Wassermann-fastness in general paralysis

The second investigation, carried out at Maudsley Hospital, London, dealt with the response to chemotherapy of the Wassermann reaction in paretics treated previously with malaria. Moore states that patients with general paresis display an unusual degree of "Wassermann-fastness". In the present investigation there was under treatment a group of 72 patients with strongly positive blood Wassermann reactions (+ 30 + ; for explanation of terminology see Mann and Partner). Of these, 56 were paretics who had undergone malaria therapy alone at least a year before ; in some cases the interval was much longer. The remaining 16 were patients who were in the hospital for their mental condition, and in whom syphilis was discovered only in the course of routine investigation ; they were probably cases of latent syphilis. The psychosis in such cases was quite unconnected with the disease, so far as could be ascertained. These non-paretics had already received chemotherapy. In most of the cases tryparsamide had been used in an average total dose of 22 grammes. The 72 patients were given an intensive four-months' course of chemotherapy. The blood Wassermann reaction was tested before, shortly after, and at four months after treatment. The last results showed that of the paretics in 38 cases the Wassermann reaction had remained positive, whereas in the group of non-paretics the number was 9.

These figures, although limited, are considered to be worthy of publication on account of the scarcity of data on the subject. It is mentioned above that a number of the serological reactions slowly became negative, spontaneously, after malaria therapy, as they do in many cases of untreated non-paretic syphilis (Bruusgaard). If these findings are confirmed by subsequent fuller investigations, we may be justified in concluding that Wassermann-fastness is a feature associated with general paretics before they receive adequate malaria therapy, but not after such treatment.

This subject would well repay further investigation. For the moment the practical deductions which may be drawn strengthen the view that the blood Wassermann reaction alone is unreliable as a guide to treatment after malaria therapy, and that the main attention should be devoted to the clinical condition and to the cerebrospinal fluid.

Summary

- (1) The clinical records of 312 general paretics were examined.
- (2) A very low incidence (3 per cent) of clinically obvious non-paretic syphilitic lesions was found.
- (3) The evidence in favour of treatment by malaria alone is reviewed.
- (4) The degree of "Wassermann-fastness" in paretics after malaria therapy was investigated. The cases so far investigated do not show any special degree of "Wassermann-fastness".

I desire to express my gratitude to Dr. W. D. Nicol, Medical Superintendent of Horton Hospital; to Dr. E. L. Hutton, who suggested and supervised this investigation ; and to the late Dr. S. A. Mann and to Mr. F. Partner of the Central Pathological Laboratory at the Maudsley Hospital, who willingly undertook the large number of serological investigations involved.

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THE MANAGEMENT AND TREATMENT OF THE LATE AND LATENT SYPHILITIC

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The management and treatment of the late and latent syphilitic is a subject that I have long felt should be discussed by this Society. I can lay no claim to any special knowledge which would enable me to speak with more authority than that of my fellow members, and I am putting forward my views in all humility in the hope that, before the end of this meeting, we may all learn something from the pooling of our experience, for this certainly is not a subject upon which anyone of us can afford to hold bigoted views.

Although the clinics in which most of us practice were originally subsidized by the Government for the diagnosis and treatment of the venereal diseases in their more acute and infectious stages, not one of us, even if it were possible, would care to practice a "split speciality" and to degenerate into professional "spirochaete spotters" and "injectioneers" of the appropriate specifics. It is because the Ministry of Health has always allowed us to care for the late syphilitic in our clinics, and because our professional colleagues continue to regard us as syphilologists in the widest sense of the word, that cases of late and latent syphilis continue to be a cumulative charge on our time, accommodation and skill.

These patients usually come under our care in one of the following ways.

(1) An obvious or suspicious lesion or circumstance is discovered by the patient's doctor or by another specialist. This may or may not be confirmed by positive blood findings.

(2) A routine serological test is found to be positive, as, for instance, in the case of a blood donor or of an expectant mother.

(3) A patient who, in the past, has had inadequate treatment for early syphilis returns after a lapse of months or years, impelled by an uneasy conscience, sometimes made still more uneasy by propaganda.

(4) A syphilitic "family skeleton" is unearthed, and the anxious spouse, parent, brother or sister comes to us for help.

TREATMENT OF LATENT SYPHILIS

Obvious late activity almost invariably is preceded by a varying period of apparent latency, so that it is convenient to commence with latent syphilis and to discuss first its treatment and management.

Diagnosis

The diagnosis of latent syphilis is one of exclusion and is always difficult and sometimes impossible to make with accuracy. It will depend largely upon the clinical experience of the examining doctor, upon negative results of radiological and cerebrospinal fluid examinations, and upon the verification by repetition of positive blood findings. All this will take time, and fortunately, except in the

* An address to the Medical Society for the Study of Venereal Diseases, 27th July 1946.